Multiplicity of Neuronal Receptors

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This presentation will discuss the general concept of multiple neuronal receptors, the chemical and biochemical basis for multiple receptors, and the various appoaches used for the elucidation of their functional diversity. It is well established that neurotransmitters, neuropeptides, and most psychotropic drugs exert their biological effects by acting on specific recognition sites, or receptors, located on neurons as well as blood vessels and neuroglia. Receptors are macromolecular complexes found throughout the membranous surfaces on the neuron as well as on various intracellular organelles, such the nuclei, endoplasmic reticulum, and mitochondria. The neuronal surface receptors, which are involved directly in neuronal excitation and communication between cells, are either post-synaptic or pre-synaptic, the former being present on the cell body or its dendritic processes and the latter on the synapse making contact with the neuronal cell body. As a nerve impulse travels down the axon of an active neuron it releases a neurotransmitter from the nerve ending (synapse) which then acts at receptors in various ways: 1) by exciting (depolarizing) a second neuron, by activating sodium conductance channels; 2) by inhibiting (hyperpolarizing), by activation of chloride channels; 3) to activate a secondary messenger (transducer) which indirectly regulates neuronal function through a metabolic cascade regulating ion conductance or the biosynthesis, release, and reuptake of neurotransmitters; or 4) by acting allosterically to potentiate or modulate another receptor subtype. A post-synaptic receptor directly controls the excitation of the neuron, while one type of pre-synaptic receptor regulates the synaptic release of a neurotransmitter directly on to the neuron and another (autoreceptor) regulates the biosynthesis of the neurotransmitter. As revealed by receptor purification-cloning, ligand binding, biochemical, and pharmacologic-electophysiologic studies, virtually all known neurotransmitters, neuropeptides, and hormones act at more than one receptor subtype. The functional significance of the brain multiple receptors is virtually unknown, and its elucidation remains one of great challenges for neuroscience research.

With the use of a simpler neuronal system, such as the mammalian superior cervical ganglion, an attempt will be made to illustrate some of the concepts outlined. Also to be discussed are recent studies in our laboratory on the functional and biochemical characteristics of multiple brain nicotinic receptors.